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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/380,377 | 09/16/1999 | NEIL J BULLEID | 39-189 | 2543 |

7590 12.04.2002

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[REDACTED] EXAMINER

WOITACH, JOSEPH T

| ART UNIT | PAPER NUMBER |
|----------|--------------|
| 1632 | |

DATE MAILED: 12/04/2002

12/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

| | |
|-------------------------------|--------------------------------|
| Application No. 09/380,377 | Applicant(s) Bulleid, N. J. |
| Examiner Joseph Woitach | Art Unit 1632 |



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on Sep 25, 2002

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) Claim(s) 31-50 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 31-46 and 48-50 is/are rejected.

7) Claim(s) 47 is/are objected to.

8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892)

4) Interview Summary (PTO-413) Paper No(s). _____

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

5) Notice of Informal Patent Application (PTO-152)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s). 1

6) Other: _____

Art Unit: 1632

DETAILED ACTION

This application is a 371 national stage filing of PCT/GB98/00468 filed 03/02/98, and claims priority to the foreign application 9704305.3 filed in the United Kingdom, 03/01/97.

Applicant's amendment filed September 25, 2002, paper number 26, has been received and entered. Claims 31-50 are pending and currently under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31-46 and 48-50 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a desired procollagen polypeptide in an isolated cell, does not reasonably provide enablement for producing pro-collagen in an animal or plant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

It is noted that upon consideration of Applicant's arguments and reconsideration of the embodiments encompassed by the claims, the rejection of claim 46, as it is drawn to isolated

Art Unit: 1632

cells is withdrawn. Further, it is noted claim 45 recites the use of a yeast cell. As noted in the basis of the rejection, embodiments of claims which drawn to practicing the method in isolated cells is not subject to the instant rejection.

With respect to the outstanding rejection, noting the eight factors set forth by the courts in *In re Wands* Applicants argue that the instant disclosure enables invention as claimed. Specifically, Applicant argues that one of skill in the art would expect failures in producing transgenic animals and plants, however, given the level of skill in the art the artisan would know how to navigate these problems and that quantity of experimentation would not be undue. Applicant points to pages 10-11 of the specification for the support and guidance of generating transgenic plants and animals, noting the preferred embodiments for expression of a particular transgene. Applicant notes that there is no working examples, however has provided a post-filing reference which includes the inventor demonstrating that transgenic mouse containing a transgene whose expression is directed to the mammary gland is capable of producing pro-collagen in the milk. In review of the nature of the invention, Applicant argues that in attempting to make transgenic plants and animals the artisan recognizes obstacles and that experimentation would be required, however the burden of experimentation is outweighed by the advantages of finally providing the desired product, *i.e.* a transgenic animal/plant. Noting several prior art references, Applicant argues that in light of the state of the art and the level of skill in the art, given the guidance of the present disclosure the artisan would be able to produce a transgenic animal and plant capable of use in the methods instantly claimed for producing pro-collagen. See

Art Unit: 1632

Applicant's amendment, pages 2-11. Applicant's arguments have been fully considered but not found persuasive.

The courts have stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in patent application. 27 USPQ2d 1662 *Ex parte Maizel*. In the instant case, upon review of the post-filing reference by John *et al.* (Nature Biotech, 1999) and references cited in Applicant's amendment, Examiner would agree that given the level of skill in the art the artisan would be able to generate a transgenic mouse wherein said mouse is capable of expressing a detectable amount of pro-collagen in the milk and to extend these observations for the generation of other transgenic mammals wherein said mammals produced detectable quantities of pro-collagen in the milk. However, the claims are much broader than simply producing a bioreactor mammal. Previously, a detailed analysis of the unpredictability of transgene behavior has been set forth. In particular, it was noted that while the methodology to generate a transgenic mammal animal was becoming routine, the behavior of the inserted transgene was not. While the teachings of Walmsley and Mylyharju support in general the ability of a recombinant pro-collagen to assemble when produced, these references clearly indicate that non-functional and non-enabled embodiments within the scope of the claims exist even for isolated cells. Applicants point to John *et al.* for support of the breadth of the instant claims, however John *et al.* also not several specific limitation for producing pro-collagen in a variety of cells. For example, John *et al.* specifically state that bacterial and yeast (claim 45)(page 385, paragraph bridging columns), and insect cells (claim 45) (page 388, tip of

Art Unit: 1632

second column and page 385, top of second column) lack the necessary enzymes needed to process the pro-collagen produced. John *et al.* note that mammalian expression systems, in particular the mammary cells of a transgenic mammal, may provide a better cell based system because the cells may contain the necessary enzymes for the processing of the recombinant proteins. Given the working example that the mammary tissue contains the necessary enzymes for the production of a pro-collagen molecule, Examiner would concede that embodiments directed to a transgenic mammal wherein the transgenic mammal produces a detectable level of pro-collagen in the milk would be found enabled. However, there is no guidance or evidence that these observations can be extended to other tissues in a mammal, or more broadly to any other animal. Further, as noted in the basis of the previous rejection, Colombatti *et al.* specifically teach that even native collagen genes from various species will not be properly processes and are not capable of forming pro-collagen molecules when expressed in various cell types (page 785; see summary in abstract). Additionally, the unpredictability of transgene behavior in plants was specifically set forth in the previous rejection, however Applicant has not provided any arguments or evidence that a plant based system contains the necessary enzymes which could produce or process pro-collagen protein.

The scope of enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). In view of the quantity of experimentation necessary to determine the parameters listed above, the lack of direction or guidance provided by the specification, the absence of working examples for the demonstration or correlation to the production of transgenic animals and plants of any

Art Unit: 1632

species, and the general unpredictable state of the art with respect to the generation of transgenic animals and plants, it would have required undue experimentation for one skilled in the art to make and/or use the claimed inventions as broadly claimed.

Thus, in view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to make and/or use the invention as claimed, and therefore, the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 31-50 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Applicant points to support for each of the limitations previously indicated in the basis of the rejection and argue that the claim is clear and does not require revision. Upon reconsideration, Examiner agrees that the limitations of the activities of the pro- α chain moieties are clear and the pending claims meet the requirements set forth under 35 USC 112, second paragraph.

Art Unit: 1632

Conclusion

No claim is allowed. Claim 47 is objected to for being dependent on a rejected claim, however would be found allowable if rewritten in independent form encompassing all the embodiments of the independent claim and any intervening claims. Claims 31-46 and 48-50 are free of the art of record, however they are subject to other rejections.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

Art Unit: 1632

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Deborah Crouch

Joseph T. Woitach

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1632